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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/098,606	TUSE, DANIEL	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 4-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1-2-03, 1-7-03, 4-17-02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 7/19/04. Claims 1-33 are currently pending in the application and are addressed herein.

Election/Restrictions

Applicant's election without traverse of Group III (claim 3) in the reply filed on 7/19/04 is acknowledged. Claims 1, 2 and 4-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/19/04.

Claim 3 is examined herein.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 4/17/02, 1/7/03 are acknowledged .The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claims Rejected Under 35 U.S.C. § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification provides the following with respect to "immuno-protection" determination:

> Immuno-protection of a host against a cancer cell is the reduced ability or inability of the cancer cell to proliferate in the host, grow in the host, metastasize in the host, cell divide in the host, attach to the host, produce one or more signs symptomatic of the cancer in the host, or kill the host. (page 48, lines 29-32).

The specification provides the following with respect to "challenging a host with a cancer cell":

> Challenging a host with a cancer cell comprises exposing the host to a sufficient number, one or more, of the cancer cell that is able to cause a tumor or lymphoma in a host of the same species that has not been introduced to any antigen of the cancer cell. (page 47, lines 12-15).

The specification provides the following with respect to "a host":

> The host may be a cell or whole organism. The cell may be part of a cell culture, a tissue, a tissue culture, or an organ. The host may be any mammalian species, such as: one important for research purposes such as a mouse, rat, hamster, rabbit, pig, goat, primate, or the like; or, one important for commercial purposes, such as a goat, sheep, cow, cattle, horse, pig, dog, cat, or the like. The host may also be a human. It will be noted that these animals come from four orders of class: Mammalia: Primata, Rodenta, Carnivora, and Artiodatyla. The host may be an animal oocyte, egg, embryo, embryonic stem cell, or any other specific animal tissue. The host may be transgenic or non-transgenic. (page 7, lines 17-25).

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claim is drawn to a method of identifying the sequence of an antigen of a cancer cell which when said antigen is expressed in a host, confers immuno-protection on the host against the cancer cell. Therefore, the nature of the Invention is a biochemical method for identifying cancer antigens that can be used as a cancer vaccine. Such a cancer vaccine would allegedly function by inducing an immuno-protective response against the cancer cells having the cancer antigen.

The breadth of the claims

The claims are very broad and encompass making a library that expresses the polypeptides expressed in a particular cancer cell, administering the library to "a group of hosts wherein each host contains one member", expressing the cancer polypeptides in the host, challenging the host with a cancer cell that expresses the potential antigen, determining which host has immuno-protection against the cancer cell and determining the sequence of the cancer antigen insert of the library.

It is respectfully pointed out that the specification indicates that the host can be a cell or a whole organism (see above). As such the claim encompasses administering the library to a groups of cells or a group of whole organisms, such that each host contains a single member of the library. It is noted that administering a library to a groups of hosts would be considered routine wherein the host is a group of cells; however, the instant claim encompasses hosts that are a group of whole organisms (i.e., animals). Considering the library may comprise many thousands of different individual members, it would not be routine to administer the library to a group of animals such that each animal comprised and expressed the cancer antigen encoded by the library member.

Furthermore, the claim encompasses challenging the host with a cancer cell. Here, the claim encompasses challenging a host cell with a cancer cell. It is not clear how a cell could be challenged with another cell, or how such a challenge could result in an immuno-protective response, as individual cells are incapable of making an immune response. Only whole animals are recognized as possibly capable of conferring an immuno-protective response.

Additionally, wherein the host can be an animal, the claims encompass xenotransplantation of cancer cell into the host. That is, the claims encompass administering a cancer cell of another species of animal into the host animal. Since the host animal must be one that is capable of making an immuno-protective response, the host animal must be one that has an intact functioning immune system (as opposed to a immuno-compromised animal). Since the animal must have an intact functioning immune system, and since the claims encompassing administering a cancer cell of another species to the host animal, one of skill in the art would readily recognize that the immuno-competent animal could have a immune response against the

cancer cell merely because the cancer cell is recognized as "foreign" to the animal because it is from another species of animal. Therefore, it is not apparent that the claimed method would work wherein the host is a cell or wherein the host is an immuno-competent animal and the cancer cell was a cancer cell from an animal of a different species.

The unpredictability of the art and the state of the prior art

The claims encompass administering a library of vectors to a group of hosts such that the vector expresses a cancer peptide/polypeptide (i.e., cancer antigen) in the host at a high enough level to induce an immune response against the cancer antigen in the host animal such that the host animal will then have immune-protection against any cell expressing that antigen (i.e., against the cancer cell). Although the general principals on which the method is based are well known in the prior art, the relevant art recognizes that inducing an immunoprotective response against a cancer antigen in an animal is not a matter of routine experimentation and there are a number of recognized obstacles that must be overcome before an a method of inducing an immuno-protective response in an animal (which is a prerequisite for the claimed method) can be considered routine.

For instance, Bodey et al. (2000) teaches: "The cancer vaccine approach to therapy is based on the notion that the immune system could possibly mount a rejection strength response against the neoplastically transformed cell conglomerate. However, due to the low immunogenicity of tumor associated antigens, down regulation of MHC molecules, the lack of adequate co stimulatory molecule expression, secretion of immune inhibitory cytokines, etc., **such expectation are rarely fulfilled**...faulty antigen presentation which could result in

tolerance induction to the antigens contained within the vaccine, and subsequent rapid tumor progression." (Page 2665, column one).

Thus, it is evident that the skilled artisan, while acknowledging the significant potential of immunotherapy for cancer, still recognizes that such therapy is neither routine nor wholly accepted. Furthermore, significant development and further guidance is necessary for its practice. Therefore, it is incumbent upon applicants to provide sufficient and enabling teachings within the specification for the instant method.

In order to enable the instant claims in light of the state of the relevant art, the applicant must provide guidance/working examples to demonstrate that the library can properly express the cancer antigens such that the cancer antigens are highly immunogenic and could provoke a useful immune response without the problems in the cited references or must provide ways to overcome the cited difficulties.

Working Examples and Guidance in the Specification

Example 3 in the specification is the only example or guidance provided relevant to the instant claimed method. Example 3 appears to be only a prophetical teaching on how one would perform the steps of the method, but does not actually indicate that the method was successfully completed. The example also does not acknowledge the caveats recognized in the art and does not disclosed any guidance to overcome these caveats. Example 3 discloses that the cDNA of a mouse fibrosarcoma is cloned into a library, and the individual members of the library are transferred into mice. The specification does not indicate how large the library is or how many mice were administered the library. Furthermore there is no guidance indicating to one of skill in the art how to administer the library to the mice such that the mice are able to properly express

a high enough level of the cancer antigen for a sufficient amount of time to even be potentially able to induce an immune response in the mouse, let alone an immuno-protective immune response against any cancer cell that expresses that antigen. The specification merely indicates that the cancer cells are administered to the mice and in those cancer cells which do not develop into tumors, the vectors are recovered and the inserts encoding the tumor antigens are sequences thus, allegedly identifying the cancer antigens that can be used to induce immunoprotection. Again the specification does not recognize, nor offer guidance to overcome the problems recognized in the art.

Quantity of Experimentation

Considering the breadth of the claim, as well as the problems associated with inducing an immunoprotective response in an animal using a cancer antigen, an enormous amount of additional experimentation would be required in order for one of skill in the art to be able to make and use the claimed invention to the full scope encompassed by the claim. For instance, additional experimentation would be required in order to determine how a cell could be challenged with a cancer cell and result in a immuno-protective response. Furthermore, additional experimentation would be required in order to determine how a non-mouse cancer cell could be administered to an immunocompetent mouse without inducing an immune response by itself. Additionally, experimentation would have to be performed in order to overcome the many caveats recognized in the art, such as the low immunogenicity of cancer antigens in general, etc.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the nature of the invention, the breadth of the claims, the problems recognized in the art, the lack of an actual working example and lack of specific guidance to overcome the problems recognized in the art and the high degree of skill required—all as a whole an not individually; it is concluded that the amount of experimentation required to perform the broadly claimed invention to the full scope encompassed by the claim is undue.

Claims Rejected Under 35 U.S.C. § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

VAGUE AND INDEFINITE

Claim 3 recites the limitation "cancer cell derived DNA sequences". The term "derived" renders the claim vague and indefinite because it is unclear if the claim encompasses: 1) "cancer" DNA sequences; or 2) DNA sequences that are not cancer sequences, but merely cancer "derived" sequences. For example, a DNA sequence derived from a cancer cell may be a DNA that is not actually found in the cancerous cell, but is one "derived" from the cancer cell. Clarification of the metes and bounds, via clearer claim language is requested.

Claim 3 recites the step of "determining which host has immuno-protection against the cancer cell" which is considered vague and indefinite. Referring to above 35 U.S.C. 112 1st

Paragraph Rejection for the definition of "immuno-protection" it is unclear what constitutes immuno-protection of a host against a cancer cell, and it is unclear how the immuno-protection is determined. For instance, the specification defines "immuno-protection" as "the reduced ability or inability of the cancer cell to... produce one or more signs symptomatic of the cancer in the host". However, the specification does not make clear the signs that are symptomatic of the cancer in the host. Additionally, in order for the determination of immuno-protection to have the "reduced ability..." (As provided for in the specification) there would be required a reference point (i.e. value/threshold/control) or prior determination of the ability of the cancer cell to "proliferate in the host, grow in the host, metastasize in the host..." Thus, it is not clear what the required characteristics or criteria are to establish a host as having immuno-protection against the cancer cell. Clarification of the metes and bounds via clearer claim language is requested.

LACK OF ANTECEDENT BASIS

Claim 3 recites the phrases "the cancer cell derived DNA sequences" (in step (a)), "the member" (in step (c)), "the cancer cell" (in step (d)). These phrases lack proper antecedent basis because said limitations are not presented prior to its utilization or it is unclear to which prior recitation the phrase is intended to refer. For instance, there is no prior recitation of "cancer cell derived DNA sequences", thus there is no antecedent basis for this phrase. Additionally, regarding the phrase "the member" in step (d), it is unclear if "the member" is intended to refer to the member of the library or to the member of the group of hosts. Similarly, with respect to the phrase "the cancer cell" in step (d), is indefinite because the preamble does not identify any

specific cancer cell, but rather encompasses "identifying the sequence of an antigen of a cancer cell". Clarification of the metes and bounds via clearer claim language is requested.

Claim Objections

Claim 3 is objected to because of the following informalities:

1) Step (c) recites, "expressing each insert, capable of expression in the host, in the host in which the member resides";

2) Step (d) recites, "challenging each of the host with the cancer cell".

These phrases appear to be grammatically incorrect, and thus are confusing. It is believed that the indicated phrases could be written more clearly. Appropriate correction is requested.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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